

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
13 October 2005 (13.10.2005)

PCT

(10) International Publication Number  
**WO 2005/095377 A1**

(51) International Patent Classification<sup>7</sup>: C07D 317/44

(74) Agent: ASTRAZENECA; Global Intellectual Property,  
S-151 85 Soderatlje (SE).

(21) International Application Number:  
PCT/GB2005/001200

(81) Designated States (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(22) International Filing Date: 29 March 2005 (29.03.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
0400873-6 31 March 2004 (31.03.2004) SE

(84) Designated States (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(71) Applicant (*for all designated States except MG, US*): ASTRAZENECA AB [SE/SE]; S-151 85 Sodertalje (SE).

(71) Applicant (*for MG only*): ASTRAZENECA UK LIMITED [GB/GB]; 15 Stanhope Gate, London, Greater London W1K 1LN (GB).

(72) Inventor; and

(75) Inventor/Applicant (*for US only*): ABEDI, Vahak [SE/SE]; AstraZeneca R & D Sodertalje, S-151 85 Sodertalje (SE).

**Published:**

— with international search report

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: CHEMICAL PROCESS

(57) Abstract: The present invention provides a process for the preparation of a compound of formula (I): wherein R<sup>1</sup> is C<sub>1-6</sub> alkyl; R<sup>2</sup> and R<sup>3</sup> are, independently, C<sub>1-6</sub> alkyl; and R<sup>4</sup> is C<sub>1-6</sub> alkyl or benzyl (wherein the phenyl ring of benzyl is optionally substituted by nitro, S (O)<sub>2</sub>(C<sub>1-4</sub> alkyl), cyano, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkoxy, C(O)(C<sub>1-4</sub> alkyl), N(C<sub>1-6</sub> alkyl)<sub>2</sub>, CF<sub>3</sub> or OCF<sub>3</sub>); the process comprising reacting a compound of formula (II): wherein R<sup>2</sup>, R<sup>3</sup> and R<sup>4</sup> are as defined above, with a suitable base; and reacting the product so formed with R<sup>1</sup>OC(O)CH<sub>2</sub>X, wherein R<sup>1</sup> is as defined above and X is chloro, bromo or iodo; wherein the process is carried out in a suitable solvent at a temperature in the range -40°C to -5°C; and wherein at least 0.2 moles of the compound of formula (II) are used in the process.

WO 2005/095377 A1